

Vaginal chemoprophylaxis in the reduction of reinfection in women with gonorrhoea

Clinical evaluation of the effectiveness of a vaginal contraceptive

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SUMMARY A clinical investigation was undertaken to determine if chemoprophylaxis in the form of a contraceptive pessary would reduce the rate of reinfection with gonorrhoea in 1245 female patients attending a venereal disease clinic. After the introduction of the pessary the reinfection rate over a 16-week period was 19% compared with 40% in the control clinic patients. It was also found that women could be motivated to use a pessary; 65% of women used pessaries before sexual intercourse at least some of the time. High reinfection rates in venereal disease clinic patients emphasise the need for improved methods of preventing reinfection. Vaginal chemoprophylaxis appears to be an alternative means of reducing gonorrhoea morbidity.

Introduction

The increasing prevalence of gonorrhoea is widely acknowledged and of increasing concern to the health professions. Of additional concern are factors such as the developing resistance of *Neisseria gonorrhoeae* to available antibiotics and the failure of current methods, such as contact tracing, to reduce the rising incidence of infections. As a result there has recently been an increase in published reports in the use of prophylactic methods for sexually transmitted infections.¹⁻⁸

Of the different methods of prophylaxis, vaginal preparations have received the most attention. Systemic and mechanical prophylaxis, while theoretically highly effective, have several disadvantages. The prophylactic use of systemic antibiotics may cause sensitisation with adverse reactions and also an increase in the number of resistant organisms. Although they avoid these side effects, condoms require the co-operation of the male partner and it is evident that this co-operation may not exist.¹

As a result research has turned to the evaluation of local methods which can be used by the female partner. Of specific interest is chemoprophylaxis using commercially available products, such as vaginal contraceptives.²⁻⁸ In-vitro studies showed

that contraceptive products indeed have the potential to kill *N gonorrhoeae*.² Further, Lee *et al*⁶ proposed that if 25% of the high-risk population consistently used a product which was 50% effective, a dramatic decrease in the prevalence of gonorrhoea could be seen within a short period of time.

These factors, together with the realisation that current management of gonorrhoea was not reducing the incidence of infections in Florida, prompted us to evaluate the potential of a chemoprophylactic vaginal contraceptive in reducing the incidence of gonorrhoea in women. The two major questions were: (a) to what extent women currently infected with gonorrhoea could be encouraged to use a pessary before sexual intercourse; and (b) whether or not chemoprophylaxis would reduce the reinfection rate in these women.

Patients and methods

This study covered two distinct phases: phase 1 (1 April to 1 October 1976) served as the pre-trial control period, during which clinic patients in two geographically separate areas (Tampa and Orlando, Florida) were managed identically. During phase 2 (1 November 1976 to 2 September 1977) vaginal pessaries were prescribed only for women attending the clinic at Tampa.

STUDY LOCATIONS

Two criteria were used to select the two study loca-

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tions; the first was similarity of sociodemographic characteristics based on census data (of special interest was the lower population quartile, which appears to be the commonest among venereal disease clinic patients, table I); and the second was an adequate number of patients to provide a true sample. To estimate gonorrhoea reinfection rates, having a standard error of no more than 3% with 90% confidence, at least 188 patients at each clinic during both phases had to be re-examined.

STUDY POPULATION

All women presenting at the two venereal diseases clinics with cervical gonorrhoea confirmed by isolation of gonococci on Thayer-Martin selective medium and who were treated with aqueous procaine penicillin G (APPG) 4.8 megaunits and probenecid 1 g were eligible for inclusion in the study. Patients were excluded if they were pregnant, wished to become pregnant, or were found to have syphilis. In addition, anyone not expecting to remain in the area for 90 days was excluded. Patients who were reinfected during the study were not re-entered.

CLINIC STAFF

Clinic staff were employed and trained specifically for the project. Training took place jointly for staff at both clinics and was conducted by personnel of the Florida Department of Health and Rehabilitative Services. The staff were supervised by experienced clinic supervisors, and retraining and clinic visits were performed periodically.

Trained interviewers questioned all prospective study patients to ascertain their eligibility for inclusion in the project and to record pertinent medical and sociodemographic information. In addition, information was obtained on previous history of gonorrhoea and the number of sexual partners in the last 90 days.

FOLLOW UP

Patients were asked to return for three cultures for gonococci and further interviews at 30-day intervals beginning one month after treatment (that is, after admission to the study); they were given appointment

cards with dates of future attendances. During re-examination, patients attending the Tampa clinic were asked how many sexual contacts they had had since the previous clinic visit and how often they had used the pessaries. Follow-up procedures were identical in both clinics. When patients failed to keep their follow-up appointments, they were telephoned or visited at home to ensure future attendance.

Before the study, established gonorrhoea control procedures in both cities were altered in three ways. Firstly, test-of-cure cultures were not performed; secondly, contact tracing of male patients with gonorrhoea was not carried out; and, thirdly, names of male sexual partners were not elicited from female patients; referral appointment cards were however distributed to the women for their contacts to attend the clinic.

The second phase of the study differed from the first only in that chemoprophylaxis was used for patients attending the clinic at Tampa; at the initial visit patients were given 24 vaginal pessaries,† instructed in the use and preventive aspects of the product, and strongly encouraged to insert the pessaries into the vagina between 15 and 60 minutes before sexual intercourse.

ADDITIONAL USE OF ANTIBIOTICS

In case study patients might have received additional antibiotics which could have affected gonococcal isolation rates patients who were treated with any medication other than APPG 4.8 megaunits (and probenecid) for any disease or condition other than gonorrhoea were excluded from the study. At follow up patients were questioned routinely about treatment for a venereal disease received elsewhere since the last visit; those reporting such treatment were also excluded from the study.

Similarly, respiratory disease in the general population during the study period could have affected the use of antibiotics. During phase 1 and phase 2, 13% and 24% more cases of respiratory

†Lorophyn contraceptive suppositories, manufactured by Eaton Laboratories, Division of Norwich Pharmacal Company. The active ingredients are: phenylmercuric acetate 0.4 mg, methylbenzethonium chloride, and methylparaben in a water-dispersible base.

TABLE I *Selected socioeconomic indicators for lowest population quartile* in the Tampa and Orlando Standard Metropolitan Statistical Areas (SMSA) (1970)*

SMSA	Median education (years)	Median income (US\$)	% Black population	% Unskilled labour
Tampa	8.9	4846	11.1	36.0
Orlando	8.7	4198	14.9	53.3

*The lower population quartile is comprised of the population falling into the lowest 25% of the Standard Metropolitan Statistical Area (SMSA) based on socioeconomic status (SES), which is a three-factor equally-weighted index (education, income, occupation). SMSA is a US Department of Commerce, Bureau of Census term which describes a county or group of counties meeting specified population criteria.

diseases respectively were reported in Orlando than Tampa (reported as influenza, influenza-like diseases, and streptococcal infections). This strongly suggests that the general use of antibiotics for these infections was no greater in Tampa than in Orlando.

The possibility that penicillin-resistant strains of gonococci could have affected the results of the study would appear to have been excluded. Since 1975, a surveillance programme has operated in Florida to screen all test-of-cure cultures for penicillinase-producing organisms. Only four such strains have been recovered, each associated with exposure in South-east Asia, and none was reported from Tampa or Orlando.

STATISTICAL METHODS

Life-table analysis was used to compare differences in cumulative reinfection rates at weekly intervals. This analysis was based on the methods described by Potter.⁹ In this analysis the assumption is made that the risk of infection may vary with time but is constant at any given point in time. Reinfections were expressed in terms of the number of infections per 100 women. Yates's correction was not used in computing χ^2 tests because of the large size of individual data cells.

Principal components analysis was used to identify associated variables. An efficient multiple regression search routine produced a model forecasting reinfection rates.

Results

During phases 1 and 2, 570 and 675 women respectively were studied at the two clinics (table II). Sociodemographic data showed strong similarities in the patients seen at both clinics during both phases (table III). Analysis of comparative sociodemographic data showed both locations had similar study populations. The sexual behaviour of female patients was also very similar during both phases and at both locations (table IV).

The percentage of women returning for at least one follow-up visit ranged from 64% to 70%. There were no sociodemographic differences between those women who did and did not return.

REINFECTION RATES

During phase 1, the control period, the cumulative reinfection rates were similar during the first six and 42% in Orlando ($\chi^2 = 0.01$, $P = 0.94$).

When chemoprophylaxis was introduced in the Tampa clinic, the reinfection rate over a 16-week period fell (fig 2). The reinfection rate of 19% in Tampa was significantly lower than the 40% rate in Orlando ($\chi^2 = 2.4$, $P = 0.12$). Interestingly, the reinfection rates were similar during the first six weeks ($\chi^2 = 0.00$, $P > 0.98$), but after that period they were significantly different ($\chi^2 = 9.46$, $P = 0.002$).

Comparisons were also made of the reinfection rate between phase 1 and phase 2 for each clinic.

TABLE II *Culture results by phase and location of patients examined and reinfected*

	Phase 1			Phase 2		
	Orlando	Tampa	Total	Orlando	Tampa	Total
No of patients attending	280	290	570	363	312	675
No of patients recultured						
First revisit	196	190		243	200	
Second revisit	96	88		85	86	
Third revisit	48	51		30	49	
Reinfected patients:						
Positive culture results at						
First revisit	31	36		34	23	
Second revisit	17	14		11	4	
Third revisit	3	2		4	0	
Cumulative reinfection rate (at 16 weeks)	42	34		40	19	
Standard error	7	4		7	4	

TABLE III *Sociodemographic characteristics of women attending clinics at Tampa and Orlando*

	Phase 1		Phase 2	
	Tampa	Orlando	Tampa	Orlando
Mean age	21.0	20.8	20.9	20.6
Non-white (%)	63.8	53.6	50.3	52.6
Married (%)	15.2	11.1	10.3	13.5
Mean education	11.2	11.0	11.3	11.3
From low socioeconomic group (%)	59.6	64.5	50.0	57.8

TABLE IV Comparison of sexual behaviour of study patients

Visit	Mean No of different sexual partners			
	Phase 1		Phase 2	
	Tampa	Orlando	Tampa	Orlando
Initial	2.0*	1.9	2.0‡	1.9
Follow up				
First	1.0†	0.9	1.1§	1.1
Second	1.0	1.0	1.1	1.1
Third	1.1	1.0	1.1	0.9

*Excludes two women who claimed 60 and 61 male partners respectively; if included mean number would be 2.4

†Excludes one woman who claimed 33 different male partners; if included mean number would be 1.3

‡Excludes one woman who claimed 36 different male partners; if included mean number would be 2.2

§Excludes one woman who claimed 30 different male partners; if included mean number would be 1.2

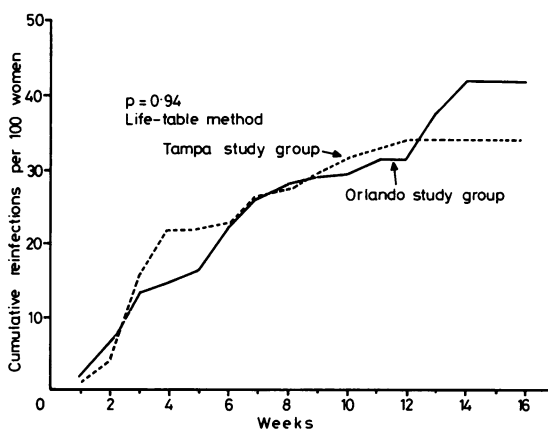


FIG 1 Reinfection rates during phase 1 (control period) in clinic patients at Tampa compared with those at Orlando

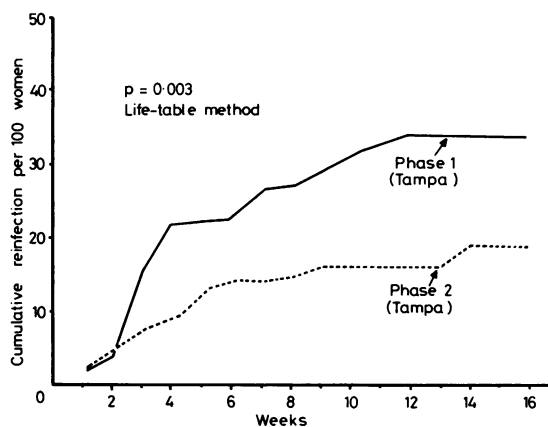


FIG 3 Reinfection rates in clinic patients at Tampa during phase 1 (no chemoprophylaxis) compared with phase 2 (chemoprophylaxis)

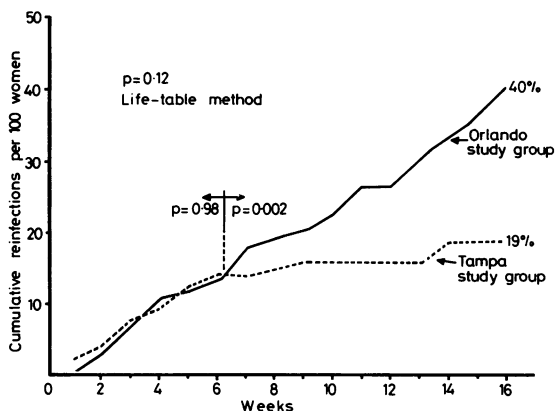


FIG 2 Reinfection rates during phase 2 (trial period) in clinic patients at Tampa compared with those at Orlando

After chemoprophylaxis had been introduced in Tampa, significantly lower reinfection rates ($\chi^2 = 9.02$, $P = 0.003$) were recorded (fig 3). There was no difference in Orlando ($\chi^2 = 2.17$, $P = 0.14$) (fig 4).

STATISTICAL FINDINGS

A principal components analysis was used to show some of the characteristics of women attending the clinic in Tampa. The first factor included young women who tended not to use the pessaries and failed to return for their follow-up appointments on time. The second factor included a high rate of use of the pessary at first follow-up visit and constant use thereafter. These women were above the average age of the study group; this finding highlights the need for greater emphasis on health education in younger women.

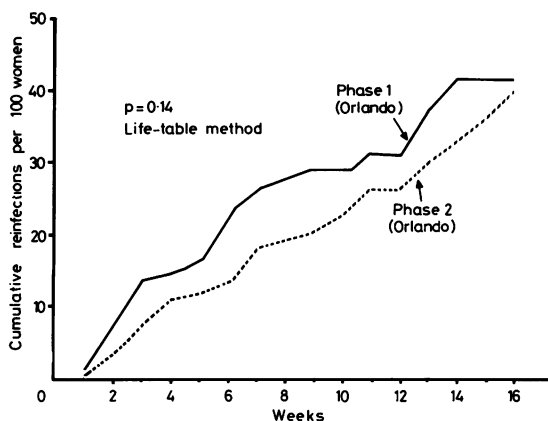


FIG 4 Reinfection rates in clinic patients at Orlando during phase 1 (no chemoprophylaxis) compared with phase 2 (no chemoprophylaxis)

Multiple regression analysis produced several models forecasting reinfection, the most efficient of which consisted of two variables. A greater number of sexual contacts during the project period and a lower educational level were found to be significant predictors ($P < 0.05$). In addition to showing that venereal disease education should be directed at those below the median educational level (11th grade) of study patients, this analysis indicates that clinic staff should interview patients who have a greater number of sexual contacts than average more intensively during subsequent interviews.

It was also seen that the women could be motivated to use a pessary; 65% of the women claimed that they sometimes used a pessary before sexual intercourse. The older patients used them more often than the younger ones.

The women attending the venereal disease clinic at Tampa during the study period constituted approximately 15% of the women in the greater Tampa area who were diagnosed as having gonorrhoea by all county physicians during the study. As expected the impact of reduced reinfection on reported gonorrhoea was minimal in the Tampa area during phase 2 compared with phase 1. Although previous gonorrhoea control procedures were also suspended at Orlando (control location), there was no significant change in the number of reported cases of female gonorrhoea for the greater Orlando area during the study.

Conclusion

The results of this study showed that reinfection rates were reduced when vaginal chemoprophylaxis was introduced, that women can be motivated to use a pessary, and that vaginal prophylaxis has a place in the control of gonorrhoea. These results are similar to those observed by Cutler *et al.*,⁸ who found that an over-the-counter vaginal contraceptive was effective in protecting against reinfection with gonorrhoea.

A third phase of the study in which chemoprophylaxis would be suspended at the Tampa clinic was planned but could not be carried out due to lack of resources. Further research in other clinics is encouraged.

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